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PATENT #14
B. Webb
8-5-03

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Applicant: O. S. Khalil, et al.

Serial No: 09/834,440

Filed: April 13, 2001

For: METHOD FOR OPTICAL MEASUREMENTS OF TISSUE TO DETERMINE DISEASE STATE OR CONCENTRATION OF AN ANALYTE

Group Art Unit: 3736

Examiner: Kremer, Matthew J.

File No.: 6800.US.O1

Date: July 21, 2003

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Kimberly A. Iorio

BRIEF ON APPEAL

Mail Stop Appeal Brief-Patents
Commissioner for Patents
P. O. Box 1450
Alexandria, VA 22313-1450

Attention: Board of Patent Appeals and Interferences

Dear Sir:

This brief is in furtherance of the Notice of Appeal filed in this application on April 21, 2003.

The fees required under 1.17(f) and any required petition for extension of time for filing this brief (two months) and fees therefor are dealt with in the accompanying TRANSMITTAL OF BRIEF ON APPEAL. This brief is being submitted in triplicate. This brief contains these items under the following headings and in the order set forth below:

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I. REAL PARTY IN INTEREST

The real party in interest is Abbott Laboratories, Abbott Park, Illinois.

II. RELATED APPEALS AND INTERFERENCES

There are no related appeals or interferences.

III. STATUS OF CLAIMS

Claims 1-18 were filed in the original application. Claims 1, 8, 9, 15, 17, and 18 were amended in an AMENDMENT AND RESPONSE mailed August 26, 2002. Claims 1-18 remain pending in the application. No claims are allowed. Claims 1-18 stand rejected. Claims 1-18 are on appeal.

IV. STATUS OF AMENDMENTS

An Amendment Under 37 C.F.R. 1.116 is being submitted herewith to correct minor errors in claims 9 and 17. This amendment has not yet been entered.

V. SUMMARY OF INVENTION

This invention provides a method for collecting optical data at two morphologically similar, substantially non-overlapping, and preferably adjacent, areas on the surface of a human tissue, while the temperature in each area is being maintained or modulated according to a temperature program. The optical data obtained are inserted into a mathematical relationship, e.g., an algorithm, that can be used to predict a disease state

(such as the diabetes mellitus disease state) or the concentration of an analyte for indicating a physical condition (such as blood glucose level).

This invention can be used to differentiate between disease status, such as, for example, diabetic and non-diabetic. The discovery underlying the method of this invention is that certain optical properties of human tissue change in response to changes in temperature of the tissue. The method involves the generation of a calibration (or training) set that utilizes the relationship between optical signals emanating from the skin under different thermal stimuli and disease status, e.g., diabetic status, established clinically. This calibration set can be used to predict the disease state of other subjects. Because thermal stimuli affect microcirculatory action within the capillary loops, the method depends upon measuring the optical properties of the tissue at different areas on the surface of the tissue, to a depth of up to two millimeters, as a function of thermal stimuli. Structural changes, as well as circulatory changes, due to a disease state are determined at two morphologically similar, but substantially non-overlapping areas on the surface of human tissue, e.g., the skin of a forearm, with each area being subjected to different temperature modulation programs.

In addition to determination of a disease state, this invention can also be used to determine the concentration of an analyte in a human tissue.

The mathematical relationship is typically established by correlating the parameter with the disease state, which is determined by invasive methods. A representative example of a disease state is diabetes. The thus-established mathematical relationship can be used to determine the disease state of a subject.

The mathematical relationship is typically established by correlating the parameter with the concentration of the analyte, which is determined by invasive methods. The thus-established mathematical relationship can be used to determine the concentration of the analyte in the tissue of a subject.

This invention also provides an apparatus for the determination of a disease state of a human subject, such as diabetes, or concentration of an analyte in a body part of a human subject, such as blood glucose level, by the method of this invention. The apparatus 10 comprises:

(a) at least one source of light 20, 22, 24, 26 capable of illuminating at least two morphologically similar, adjacent, not substantially overlapping areas of the body part (A1, A2) with light;

(b) at least one light collecting element 46, 48, 50, 52 to collect light re-emitted from the at least two areas of the body part;

(c) a detector 60 for measuring the intensity of the re-emitted light collected at the two areas of the body part; and

(d) a controller 66 for controlling the temperature of the at least two areas of the body part simultaneously by means of temperature programs.

VI. ISSUES

1. Are claims 9-18 unpatentable under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention?

2. Are claims 1-4, 6-7, 9-12, 14, and 16-18 unpatentable under 35 U.S.C. § 102 (b) as being anticipated by U. S. Patent 5,978,691 to Mills?

3. Are claims 5, 8, 13, and 15 unpatentable under 35 U.S.C. § 103 (a) as being obvious over U.S. Patent 5,978,691 to Mills as applied to claims 1 and 9?

VII. GROUPING OF CLAIMS

Claims 1-16 stand or fall together. Claims 17 and 18 are separate from claims 1-16.

VIII. ARGUMENT

Rejection Under 35 U. S. C. § 112

Issue 1

This ground of rejection was addressed in the AMENDMENT AND RESPONSE mailed August 26, 2002 by the amendments to claims 9 and 17.

Rejection Under 35 U.S.C. § 102

Issue 2

All of the claims of the present application specify that (a) at least one optical property at a first area on a body part of a human subject is measured to obtain a first set of data, the first area being subjected to a first temperature program; and (b) at least one optical property at a second area on the body part is measured to obtain a second set of data, the second area being subjected to a second temperature program, the second temperature program being different from the first temperature program, the second area of the body part being morphologically similar to, adjacent to, but not substantially overlapping with the first area of the body part.

As shown in FIGS. 5a and 6 of Mills, the device and method employs a single area of a body part. In the present invention, the method calls for the use of two adjacent areas of a body part. Accordingly, these figures and the discussion accompanying them do not anticipate any of the claims of this application.

As shown in FIGS. 5b, 5c, 7, and 8 of Mills, the device and method employ a plurality of finger probes. In FIG. 5b, probe 26 is attached to one finger and probe 27 is attached to another finger. In FIG. 5c, probe 32 is attached to one finger, probe 34, is attached to a second finger, and probe 36 is attached to a third finger. FIGS. 7 and 8 illustrate a plurality of finger probes. Each individual finger constitutes a separate body part. In claims 1,

9, and 17, as amended, and the claims depending from claims 1, 9, and 17, (a) at least one optical property is measured at a first area on a body part of the human subject to obtain a first set of data, the first area being subjected to a first temperature program; and (b) at least one optical property is measured at a second area on the body part of the human subject to obtain a second set of data, the second area being subjected to a second temperature program, the second temperature program being different from the first temperature program, the second area of the body part being morphologically similar to, adjacent to, but not substantially overlapping with the first area of the body part. In FIGS. 5b, 5c, 7, and 8 of Mills, separate temperature programs are run on separate body parts, while in the claims of this application, separate temperature programs are run on the same body part, but the areas on the body part must be morphologically similar, adjacent, but not substantially overlapping.

In Mills, there are several statements that further serve to distinguish the method and apparatus of Mills from the method and apparatus of this invention. In column 7, lines 58-59, Mills states:

> "Thus, the probes could be on fingers, toes, lips, etc., or any combinations of these."

In column 8, lines 1-3, Mills states:

> "Similarly, while the present invention describes the use of transillumination, it will be appreciated that reflectance spectrophotometry may be alternatively employed."

In column 9, lines 7-10, Mills states:

> "Detection of the light signal at a distinct point (normally opposing surface) is made and the relative absorbance and extinction of the signal is calculated."

The first statement shows that Mills contemplates using combinations of body parts, but does not require that the method be performed with a single body part. Furthermore, this first statement shows that Mills never contemplated the requirement that the measurements must be made in adjacent areas on the body part selected. The second statement equates transillumination with reflectance. In the present invention, transillumination is unworkable. To perform measurements by transillumination, light must go through the entire body part. The temperature of the entire body part through which light is transmitted, in a transillumination mode, will be dominated by the body core temperature. Accordingly, the temperature programs recited in the claims will not be effective. In addition, in the case where light goes through the entire body part, it will be nearly impossible to ensure that both the first and second areas of the body part will be morphologically similar. The third statement, like the second statement, calls for the use of non-adjacent areas for measurement, which is excluded by the claims of this application.

Thus, it is clear that Mills does not anticipate claims 1-4, 6-7, 9-12, 14, and 16-18 or any other claim of this application.

Rejection Under 35 U.S.C. § 103

Issue 3

Claim 8 specifies that the population comprises a first sub-population comprising a sufficient number of human subjects in the disease state and a second sub-population comprising a sufficient number of human subjects not in the disease state. Mills does not disclose or suggest the division of the population of human subjects into two sub-populations. Furthermore, Mills does not disclose or suggest that the at least one optical property is measured at a first area and at a second area on a body part of the human subject to obtain a first set of data and a second set of data, respectively, and that the second area of the body part is morphologically similar to, adjacent to, but not substantially overlapping with the first area of the body part.

Claim 15 specifies that that the at least one optical property is measured at a first area and at a second area on a body part of the human subject to obtain a first set of data and a second set of data, respectively, and that the second area of the body part is morphologically similar to, adjacent to, but not substantially overlapping with the first area of the body part. Mills does not disclose or suggest that the at least one optical property is measured at a first area and at a second area on a body part of a human subject to obtain a first set of data and a second set of data, respectively, and that the second area of the body part is morphologically similar to, adjacent to, but not substantially overlapping with the first area of the body part.

Claims 5 and 13 merely involve the sequence of measuring steps (a) and (b). While Mills discloses the sequence of steps set forth in claims 5 and 13, Mills fails to disclose or suggest that the at least one optical property is measured at a first area and at a second area on a body part of the human subject to obtain a first set of data and a second set of data, respectively, and that the second area of the body part is morphologically similar to, adjacent to, but not substantially overlapping with the first area of the body part.

The statement at page 7, lines 58-59 of Mills shows that Mills contemplates using combinations of body parts, but does not require that the method be performed with a single body part. Furthermore, this statement shows that Mills never contemplated the requirement that the measurements must be made in adjacent areas on the body part selected. The statement at page 8, lines 1-3 of Mills equates transillumination with reflectance. In the present invention, transillumination is unworkable. To perform measurements by transillumination, light must go through the entire body part. The temperature of the entire body part through which light is transmitted, in a transillumination mode, will be dominated by the body core temperature. Accordingly, the temperature programs recited in the claims will not be effective. In addition, in the case where light goes through the entire body part, it will be nearly impossible to ensure that both the first and second areas of the body part will be morphologically similar. The statement at page 9, lines 7-10 of Mills, like the statement at page 8, lines 1-3 of Mills, calls for the use of non-adjacent areas for measurement, which is excluded by the claims of this application.

Thus, Mills does not render claims 5, 8, 13, and 15, or any other claim of this application, obvious to one of ordinary skill in the art.

Reasons for Separating Claims 1-16 from Claims 17-18

Claims 1-16 relate to a method for the determination of a disease state in a human subject (claims 1-8) and to a method for determining concentration of an analyte in a body part (claims 9-16). Claims 17-18 relate to an apparatus capable of carrying out the methods recited in claim 1-16. However, the apparatus may be capable of carrying out additional methods other than those recited in claims 1-16. Because the scope of claims 17-18 may be broader than the scope of claims 1-16, it is requested that claims 1-16 be separated from claims 17-18.

CONCLUSION

In view of the foregoing, it is submitted that claims 1-18 are in condition for allowance, and it is requested that the Final Rejection be reversed.

Respectfully submitted,
O.S. Khalil, et al.

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ABBOTT LABORATORIES
Telephone: (847) 937-6182
Facsimile: (847) 938-2623

David L. Weinstein
Registration No. 28,128
Attorney for Applicants

APPENDIX OF CLAIMS

The text of the claims on appeal is:

1. (Once amended) A method for the determination of a disease state in a human subject, said method comprising the steps of:

(a) measuring at least one optical property at a first area on a body part of said human subject to obtain a first set of data, said first area being subjected to a first temperature program;

(b) measuring at least one optical property at a second area on said body part to obtain a second set of data, said second area being subjected to a second temperature program, said second temperature program being different from the first temperature program, said second area of said body part being morphologically similar to, adjacent to, but not substantially overlapping with said first area of said body part;

(c) inserting said first set of data and said second set of data into a mathematical relationship to calculate a mathematical output; and

(d) comparing said mathematical output to a category selector to determine said disease state of said human subject.

2. The method of claim 1, wherein said optical properties are measured with light having a wavelength ranging from about 400 nm to about 2000 nm.

3. The method of claim 1, wherein said optical properties are measured by a diffuse reflectance technique.

4. The method of claim 1, wherein measuring steps (a) and (b) are performed simultaneously.

5. The method of claim 1, wherein measuring steps (a) and (b) are performed sequentially.

6. The method of claim 1, wherein said temperature programs employ temperatures ranging from about 10 °C to about 45 °C.

7. The method of claim 1, wherein said disease state is selected from the group consisting of diabetic state, dermal disease state, neoplasmic disease state, and vascular disease state.

8. (Once amended) The method of claim 1, wherein said mathematical relationship of step (c) is derived by a method comprising the steps of:

(a) providing a population comprising a sufficient number of human subjects to establish a category selector, said population comprising a first sub-population comprising a sufficient number of human subjects in said disease state and a second sub-population comprising a sufficient number of human subjects not in said disease state;

(b) for each of said number of human subjects in said population:

(1) measuring at least one optical property at a first area on a body part of said human subjects to obtain a first set of data, said first area being subjected to a first temperature program;

(2) measuring at least one optical property at a second area on said body part of said human subjects to obtain a second set of data, said second area being subjected to a second temperature program, said second temperature program being different from the first temperature program, said second area of said body part being morphologically similar to, adjacent to, but not substantially overlapping with said first area of said body part; and

(c) establishing a mathematical relationship between (i) said optical properties of said first set of data and said second set of data and (ii) said disease state.

9. (Once amended) A method for determining concentration of an analyte in a body part, said method comprising the steps of:

(a) measuring at least one optical property at a first area on said body part to obtain a first set of data, said first area being subjected to a first temperature program;

(b) measuring at least one optical property at a second area on said body part to obtain a second set of data, said second area being subjected to a second temperature program, said second temperature program being different from the first temperature program, said second area of said body part being morphologically similar to said first area of said body part, said second area of said body part not substantially overlapping with said first area of said body part, and said second area of said body part being adjacent to said first area of said body part; and

(c) inserting said first set of data and said second set of data into a mathematical relationship to calculate said concentration of said analyte.

10. The method of claim 9, wherein said optical properties are measured with light having a wavelength ranging from about 400 nm to about 2000 nm.

11. The method of claim 9, wherein said optical properties are measured by a diffuse reflectance technique.

12. The method of claim 9, wherein measuring steps (a) and (b) are performed simultaneously.

13. The method of claim 9, wherein measuring steps (a) and (b) are performed sequentially.

14. The method of claim 9, wherein said temperature programs employ temperatures ranging from about 10 °C to about 45 °C.

15. (Once amended) The method of claim 9, wherein said mathematical relationship of step (c) is derived by a method comprising the steps of:

(a) providing a population comprising a sufficient number of human subjects to establish a statistically meaningful mathematical relationship;

(b) for each of said number of human subjects in said population:

(1) measuring at least one optical property at a first area on said body part to obtain a first set of data, said first area being subjected to a first temperature program;

(2) measuring at least one optical property at a second area on said body part to obtain a second set of data, said second area of said body part being subjected to a second temperature program, said second temperature program being different from the first temperature program, said second area of said body part being morphologically similar to said first area of said body part, said second area of said body part not substantially overlapping with said first area of said body part, and said second area of said body part being adjacent to said first area of said body part; and

(c) establishing a mathematical relationship between (i) said optical properties of said first set of data and said second set of data and (ii) said concentration of analyte.

16. The method of claim 9, wherein said analyte is selected from the group consisting of glucose, hemoglobin, hematocrit value, tissue water content, urea, and billirubin.

17. (Once amended) An apparatus for determining a disease state of a human subject or concentration of an analyte in a body part of a human subject, said apparatus comprising:

(a) at least one source of light capable of illuminating at least two morphologically similar, adjacent, not substantially overlapping areas of said body part with light;

(b) at least one light collecting element to collect [collecting] light re-emitted from said at least two areas of said body part;

(c) a detector for measuring the intensity of said re-emitted light collected at said two areas of said body part; and

(d) a controller for controlling the temperature of said at least two areas of said body part simultaneously by means of temperature programs.

18. (Once amended) The apparatus of claim 17, further including (e) a computer for correlating the intensity of the re-emitted light collected at said at least two areas of said body part with said concentration of an analyte or said disease state, provided that said at least two areas of said body part are morphologically similar, adjacent, and substantially non-overlapping.